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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/865,627

05/25/2001

M. Kathleen Kerr

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20583

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08/10/2004

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NEW YORK, NY 10017

EXAMINER

MORAN, MARJORIE A

ART UNIT

PAPER NUMBER

1631

DATE MAILED: 08/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

9/14

<b>Office Action Summary</b>	<b>Application No.</b> 09/865,627	<b>Applicant(s)</b> KERR ET AL.	
	<b>Examiner</b> Marjorie A. Moran	<b>Art Unit</b> 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 24 May 2004.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-34 is/are pending in the application.
- 4a) Of the above claim(s) 11,12,25 and 26 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-10,13-24 and 27-34 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 24 May 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

***Election/Restrictions***

Claims 11-12 and 25-26 are again withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected method, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in a paper filed 9/22/03.

This application contains claims 11-12 and 25-26, drawn to an invention nonelected with traverse in a paper filed 9/22/03. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

An action on the merits of elected claims 1-10, 13-24 and 27-34 follows.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. All rejections and objections not reiterated below are hereby withdrawn.

***Drawings***

The drawings filed 5/24/04 are acceptable to the examiner.

***Specification***

In view of applicant's statement in the response filed 5/24/04, it is recognized that applicant does not intend to have the hyperlinks of the specification be active links. These hyperlinks will be inactivated when preparing the text to be loaded onto the USPTO web database.

***Claim Rejections - 35 USC § 101***

Claims 1-10, 23 and 27-33 are again rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Applicant's arguments filed 5/24/04 have been fully considered but they are not persuasive. In response to applicant's arguments that "correlations", as identified in the claimed methods, represent a concrete, tangible, and useful result, it is noted that the claims do not recite identification of any "correlations". Claims 1 and 13 recite final steps of "estimating... interaction effects" based on a plurality of averages from a microarray dataset and "factor effects" estimated in a previous step. As both the "factor effects" and "interactions" are limited to be related to a microarray experiment, it is unclear whether the "correlations" argued by applicant are the "interaction effects" or the "factor effects." Further, it is unclear from the arguments what is supposed to be "correlated" with what. In addition, the intended result of the methods (estimation of some kinds of "effects") is neither concrete nor tangible, and does not appear to be useful to one skilled in the art, as previously set forth and reiterated below, in the utility rejection. Applicant argues that specific examples of correlations (e.g. "cleaning up" or filtering data represents a concrete, tangible and useful result. No step of filtering data or any specific limitations with regard to partitioning light intensities are recited in the instant claims, therefore applicant's arguments are not persuasive. Applicant is reminded that limitations from the specification (e.g. examples) can not be "read into" the claims. While the specification may provide support for particular embodiments, it is noted that the CLAIMED subject matter must be statutory.

The claims merely recite steps of data manipulation, on a dataset of unknown provenance (a microarray is merely an arrangement in space, and does not describe or limit the dataset resulting therefrom), and do not produce a concrete, tangible, and

useful result. For these reasons, and those previously set forth, the rejection is maintained.

Claims 1-10, 13-24 and 27-34 are again rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. Applicant's arguments filed 5/24/04 have been fully considered but they are not persuasive. In response to applicant's arguments that "correlations", as identified in the claimed methods, represent a concrete, tangible, and useful result, it is noted that the claims do not recite identification of any "correlations". Claims 1 and 13 recite final steps of "estimating... interaction effects" based on a plurality of averages from a microarray dataset and "factor effects" estimated in a previous step. As both the "factor effects" and "interactions" are limited to be related to a microarray experiment, it is unclear whether the "correlations" argued by applicant are the "interaction effects" or the "factor effects." Further, it is unclear from the arguments what is supposed to be "correlated" with what.

While steps of statistical manipulation may be of interest to one skilled in the art, the statistical manipulation itself is not a utility under 35 USC 101. In response to examples set forth in the arguments, applicant is again reminded that the CLAIMED invention must have utility. No steps of filtering or partitioning data are recited in the instant claims. No dependant and/or independent variables are recited in the claims. Applicant is also reminded that the results of claimed method must be of "immediate benefit" to the public and/or to a skilled practitioner in the art. See MPEP 2107.01, and the analyses of utility in *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (1966) and *In re Ziegler*, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993).

The examiner maintains that a claim which merely recites estimating the effects of an unknown variable on other variables, where the variables are not identified, would

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not have a utility as further research would be required to determine what the effect is.

For the reasons previously set forth and set forth above, the rejection is maintained.

***Claim Rejections - 35 USC § 112-1***

Claims 1-10, 13-24 and 27-34 are again rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is a LACK OF ENABLEMENT rejection.

The claims are not enabled because neither the instant specification nor the prior art teach how to determine effects of factors and interactions on an unknown entity. The claims are directed to a method, and a system and medium for running the method, of estimating the effects of factors and interactions of factors in a gene expression microarray experiment, but do not identify what the effects themselves are nor what the effects are to be directed toward or what the effects are to act on (i.e. the claims do not recite WHAT is affected).

Applicant's arguments filed 5/24/04 have been fully considered but they are not persuasive. Applicant argues that the scope of invention is broad enough to cover "any choice or combination of factors" and that "one of skill in the art must decide, prior to the use of the claimed methods, the goal of the experiment." This appears to be an admission that factors and other experimental design elements must be chosen and/or estimated BEFORE the instant method can be performed. Having to guess at experimental design represents undue experimentation. Applicant then argues that once an experiment is designed and performed, statistical analysis of the resulting data may be performed using the instant method. It is noted, however, that the instant claims

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recite a method of estimating effects between factors of an experiment "that generates a microarray dataset", which limits the method to one wherein statistical analysis is performed BEFORE the experiment takes place.

As previously set forth, the state of the prior art is such that a method of analysis of variance for gene expression microarray data, similar to that disclosed, is known (See KERR et al. IDS ref: J. Comp. Biol. (2000) vol. 7, pages 819-837). However, the method of prior art also requires that "effects" be identified (e.g. dye effects or variety effects) in order to be calculated/estimated (see e.g. pages 9-10). Neither the instant specification nor the prior art provide guidance on how to estimate unknown effects or known effects on an unknown recipient. As taught by KERR et al. (supra), as more variables are added to a model, the degrees of freedom expand until it becomes difficult to predict the effects for all variables. Therefore, unless variables are explicitly identified and a decision made to include or exclude particular combinations of variables (i.e. interactions between SPECIFIC variables), effects can not be estimated (i.e. effects are completely confounded). Applicant admits, as set forth above, that the claims are quite broad. Thus, due to the high degree of uncertainty in the art for estimating effects where the effects and/or variables are not identified, the claims are not enabled by the teachings of the prior art.

For the reasons previously set forth and set forth above, the examiner maintains that it would require undue experimentation for one skilled in the art to practice the claimed methods, and maintains the rejection.

***Claim Rejections - 35 USC § 112-2***

Claims 1-10, 13-24, and 27-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 13 recite a method and system for estimating “the effects” of factor and interactions of factors. Those skilled in the art generally estimate or determine an effect OF something ON something else. It is unclear what applicant intends to estimate an effect ON, therefore the claims are indefinite. Applicant did not amend the claims nor set forth any arguments to overcome this rejection, therefore the rejection is maintained.

Claims 1 and 13 recite a method for estimating effects in a gene expression microarray experiment “which generates a microarray dataset”. Applicant argues that the change from “generating” to “which generates” makes it clear that the experiment “generates a dataset.” It is still unclear, however, if applicant merely intends to recite an intended use for the gene expression microarray of lines 2-3 of each claim, or intends to recite a method of generating a microarray dataset, or intends some other limitation. If applicant intends to recite an intended use, then it is noted that the “use” does not structurally limit the microarray dataset. If applicant intends to limit the method/program to one wherein a microarray dataset is generated, then this limitation should be recited as positive, active method steps. Applicant is reminded that such steps must be fully supported and enabled by the specification.

Claims 2, 3, 14, and 15 limit a factor to be “characterized by” a number of levels. It is unclear if applicant intends the factors to comprise a number of levels, to be identified by number of levels, to be associated with a number of levels, etc. Use of the term “characterized by” renders the limitation intended for a factor unclear, therefore the claims are indefinite. It is noted that the indefiniteness was not over whether applicant



intended a single level or a "number of levels" but was based on confusion over WHAT the relationship between a factor and the "levels" is intended to be. As the claim amendments do not clarify the intended relationship, the claims are still indefinite, and the rejection is maintained.

### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (571) 272-0720. The examiner can normally be reached on Mon. to Wed, 7:30-4; Thurs 7:30-6; Fri 7-1 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571)272-0722. The fax phone

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number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marjorie A. Moran  
Primary Examiner  
Art Unit 1631

*Marjorie A. Moran*  
8/19/04